

Cerebral palsy research news

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Interventions and Management

1. Distal level in scoliosis surgery for non-ambulatory patients with cerebral palsy: is L5 an option? A case series study

Ruben Alejandro Morales Ciancio, Jonathan Lucas, Stewart Tucker, Thomas Ember, Mark Harris, Edel Broomfield

Spine Deform. 2023 Jul 10. doi: 10.1007/s43390-023-00722-w. Online ahead of print.

Purpose: This study aimed to determine the radiographic outcomes of patients with cerebral palsy (CP) who underwent posterior spinal fusion from T2/3 to L5 at two quaternary hospitals. Methods: From January 2010 to January 2020, 167 non-ambulatory patients with CP scoliosis underwent posterior spinal fusion using pedicle screws from T2/3 to L5 in both centers, with a minimum of 2 years follow-up (FU). Radiological measurements and chart reviews were performed. Results: A total of 106 patients aged 15.6 ± 0.4 years were included. None of the patients was lost to FU. All patients had significant correction of the Cobb angle (MC) and pelvic obliquity (PO), thoracic kyphosis (TK), and lumbar lordosis (LL), without loss of correction at the last FU (LFU). The mean values for preoperative, immediate postoperative, and LFU were MC 93.4°, 37.5°, and 42.8°; PO 25.8°, 9.9°, and 12.7°; TK 52.2°, 44.3°, and 45°; and LL - 40.9°, - 52.4°, and - 52.9°, respectively. Higher residual PO at LFU was associated with more severe MC and PO baselines, lower implant density, and an apex located at L3. Conclusions: CP scoliosis and PO can be corrected, and this correction is maintained over time with posterior spinal fusion using pedicle screws, with L5 as the lowest instrumented vertebra. Larger preoperative MC and PO values associated with the apex at L3 appear to be related to residual PO. Comparative large-scale studies of patient-related clinical outcomes are required to determine whether this intervention is associated with improved surgical outcomes and reduced complication rates.

PMID: 37429979

2. Selective dorsal rhizotomy in non-ambulant children with cerebral palsy: a multi-center prospective study

Conor S Gillespie, Benjamin J Hall, Alan M George, Dawn Hennigan, Christine Sneade, Stephanie Cawker, Adikarige Haritha Dulanka Silva, Michael Vloeberghs, Kristian Aquilina, Benedetta Pettorini

Childs Nerv Syst. 2023 Jul 13. doi: 10.1007/s00381-023-06062-4. Online ahead of print.

Purpose: Assess the effects of selective dorsal rhizotomy (SDR) on motor function and quality of life in children with a Gross Motor Function Classification System (GMFCS) level of IV or V (non-ambulatory). Methods: This is a prospective, observational study in three tertiary neurosurgery units in England, UK, performing SDR on children aged 3-18 with spastic diplegic cerebral palsy, and a GMFCS level of IV or V, between 2012 and 2019. The primary outcome measure was the change in the 66-item Gross Motor Function Measure (GMFM-66) from baseline to 24 months after SDR, using a linear mixed effects model. Secondary outcomes included spasticity, bladder function, quality of life, and pain scores. Results: Between 2012 and 2019, 144 children who satisfied these inclusion criteria underwent SDR. The mean age was 8.2 years. Fifty-two percent were female. Mean GMFM-66 score was available in 77 patients (53.5%) and in 39 patients (27.1%) at 24 months after SDR. The mean increase between baseline and 24 months post-SDR was 2.4 units (95% CI 1.7-3.1, p < 0.001, annual change 1.2 units). Of the 67 patients with a GMFM-66 measurement available, a documented increase in gross motor function was seen in 77.6% (n = 52). Of 101 patients with spasticity data available, mean Ashworth scale decreased after surgery (2.74 to 0.30). Of patients' pain scores, 60.7% (n = 34) improved, and 96.4% (n = 56) of patients' pain scores

remained the same or improved. Bladder function improved in 30.9% of patients. Conclusions: SDR improved gross motor function and reduced pain in most patients at 24 months after surgery, although the improvement is less pronounced than in children with GMFCS levels II and III. SDR should be considered in non-ambulant patients. PMID: 37439914

3. Safety and Efficacy of Botulinum Toxin Type A in Children With Spastic Cerebral Palsy Aged <2 Years: A Systematic Review

Hongyi Yang, Shiwei Chen, Jiaqi Shen, Yijing Chen, Minlin Lai, Linfei Chen, Suzhen Fang

Review J Child Neurol. 2023 Jul 10;8830738231183484. doi: 10.1177/08830738231183484. Online ahead of print.

In this study, we reviewed the safety and efficacy of botulinum toxin type A (BoNT-A) injection with respect to motor development in children with spastic cerebral palsy aged <2 years. Randomized controlled trials of BoNT-A published between July 1993 and May 2021 were searched in PubMed, WANFANG, CNKI (Chinese National Knowledge Infrastructure), and Cochrane Library Central Register of Controlled Trials using keywords "Botulinum Toxin," "cerebral palsy," "nao xing tan huan," "nao tan," and "rou du du su." The 11-item PEDro Scale was used to rate the quality of all the identified studies. Twelve studies, involving 656 subjects, met the inclusion criteria, and of these, 2 involved patients aged <2 years. Treatment safety was assessed based on adverse event (AE) number and frequency, and efficacy was assessed based on spasticity, range of movement, and motor development. We observed that 3 self-limiting adverse events that were frequently reported included weakness, dysesthesia of the skin, and pain at the injection site. Moreover, there was a significant decrease in the incidence of spasticity and a notable improvement in the range of movement of BoNT-A-treated patients. Therefore, BoNT-A injection shows great safety and efficacy in the treatment of children with cerebral palsy aged <2 years.

PMID: 37431191

4. Acute and Long-Term Changes in Blood-Borne Biomarkers in Response to Dynamic Standing in Nonambulant Children With Cerebral Palsy

Tibor V Varga, Åsa Andersson, Katarina Lauruschkus, Åsa B Tornberg

Pediatr Exerc Sci. 2023 Jul 11;1-8. doi: 10.1123/pes.2022-0093. Online ahead of print.

Purpose: To investigate acute and long-term changes in hormonal and inflammatory biomarkers in nonambulant children with cerebral palsy in response to dynamic standing exercise. Methods: Fourteen children with severe cerebral palsy were recruited. Anthropometrics and body composition measures were obtained. Physical activity levels before the study were assessed using hip-worn accelerometry. All children underwent a 30-minute dynamic standing exercise using the Innowalk standing aid. Respiratory data during exercise were collected using indirect calorimetry. Blood samples were collected before and after exercise. Blood samples were also obtained after two 16-week exercise protocols, in a resting state. Hormonal and inflammatory metabolites were measured from blood serum/plasma, and acute and long-term changes in biomarker levels were assessed using Wilcoxon signed-rank tests. Results: Of the 14 children at baseline, all had slightly/moderately/severely elevated C-reactive protein and cortisol levels. C-reactive protein levels were decreased following a 30-minute bout of dynamic standing (before exercise: 53 mg/L [interquartile range: 40-201]; after exercise: 39 mg/L [interquartile range: 20-107]; P = .04). Conclusions: We show that several hormonal and inflammatory biomarkers are dysregulated in children with cerebral palsy. Our preliminary results from a small, but deep-phenotyped prospective cohort indicate acute and long-term alterations of several biomarkers in response to exercise.

PMID: 37433523

5. Effect of Swiss ball stabilization training on trunk control, abdominal muscle thickness, balance, and motor skills of children with spastic cerebral palsy: A randomized, superiority trial

Forouzan Rastgar Koutenaei, Shohreh Noorizadeh Dehkordi, Malek Amini, Shabnam ShahAli

Arch Phys Med Rehabil. 2023 Jul 11;S0003-9993(23)00345-3. doi: 10.1016/j.apmr.2023.05.011. Online ahead of print.

Objectives: To compare the effects of Swiss ball stabilization training (SBST) and stable surface stabilization training (SSST) on the trunk control, abdominal muscle thickness, balance, and motor skills of children with spastic cerebral palsy (CWSCP). Design: single-blind, randomized superiority trial. Setting: general community and referral center. Participants: Thirty CWSCP, aged 6-12 years, with Gross Motor Function Classification System (GMFCS) levels I-III were randomly assigned to the SBST and SSST groups. Interventions: The participants were randomized to receive either SBST or SSST for five weeks, three days a week. Outcome measures: The Trunk Control Measurement Scale (TCMS), abdominal muscle thickness, Pediatric Balance Scale (PBS), standing and walking sections of Gross Motor Function Measure (GMFM-88), and mobility section of the Pediatric Evaluation of Disability Inventory (PEDI) were assessed. Results: After five weeks of the intervention and nine weeks of follow-up, the SBST group showed statistically significant improvements in the TCMS, GMFM-88, PEDI, thickness

of the internal oblique muscle at rest and contraction, and thickness of the transverse abdominis muscle at rest and contraction compared to the SSST group (P<0.0001). Contrarily, the thickness of the external oblique muscle increased statistically significantly in the SSST group compared to the SBST group after five weeks of the intervention and nine weeks of follow-up both at rest (P<0.0001 and P=0.0001, respectively) and contraction (P=0.015 and P=0.017, respectively). No statistically significant difference was found between the groups regarding the PBS score after five weeks of intervention. Conclusion: The SBST could improve the trunk control, balance, and motor skills of CWSCP and increase the thickness of local abdominal muscles. Also, SBST was more effective than SSST for CWSCP.

PMID: 37442218

6. Ex vivo adult stem cell characterization from multiple muscles in ambulatory children with cerebral palsy during early development of contractures

M Corvelyn, J Meirlevede, J Deschrevel, E Huyghe, E De Wachter, G Gayan-Ramirez, M Sampaolesi, A Van Campenhout, K Desloovere, D Costamagna

Differentiation. 2023 Jul 12;133:25-39. doi: 10.1016/j.diff.2023.06.003. Online ahead of print.

Cerebral palsy (CP) is one of the most common conditions leading to lifelong childhood physical disability. Literature reported previously altered muscle properties such as lower number of satellite cells (SCs), with altered fusion capacity. However, these observations highly vary among studies, possibly due to heterogeneity in patient population, lack of appropriate control data, methodology and different assessed muscle. In this study we aimed to strengthen previous observations and to understand the heterogeneity of CP muscle pathology. Myogenic differentiation of SCs from the Medial Gastrocnemius (MG) muscle of patients with CP (n = 16, 3-9 years old) showed higher fusion capacity compared to age-matched typically developing children (TD, n = 13). Furthermore, we uniquely assessed cells of two different lower limb muscles and showed a decreased myogenic potency in cells from the Semitendinosus (ST) compared to the MG (TD: n = 3, CP: n = 6). Longitudinal assessments, one year after the first botulinum toxin treatment, showed slightly reduced SC representations and lower fusion capacity (n = 4). Finally, we proved the robustness of our data, by assessing in parallel the myogenic capacity of two samples from the same TD muscle. In conclusion, these data confirmed previous findings of increased SC fusion capacity from MG muscle of young patients with CP compared to age-matched TD. Further elaboration is reported on potential factors contributing to heterogeneity, such as assessed muscle, CP progression and reliability of primary outcome parameters.

PMID: 37451110

7. Adaptation and Validation of a Serious Game for Motor Learning Training in Children with Cerebral Palsy

Juan D Bautista, Francisco J Perales, Silvia Ramis, Pedro Montoya, Inmaculada Riquelme

Games Health J. 2023 Jul 14. doi: 10.1089/g4h.2023.0082. Online ahead of print.

Objective: Children with cerebral palsy (CP) present motor learning disorders and somatosensory dysfunction. Although many protocols use videogames in children with CP, few apply or examine motor learning principles. This study aims at (1) implementing therapist-user-designer collaboration in adapting a videogame to the principles of motor learning and the characteristics of users with CP, and (2) piloting the effectiveness of these adaptations by analyzing the achievement of motor learning parameters (learning rate acquisition, retention, and transfer to motor and somatosensory function). Materials and Methods: Periodical interprofessional meetings conducted to the adaptation of a videogame, requiring the control of a joystick for traveling through a maze, to motor learning principles. In a pilot validation, effects in unilateral upper limb function, gross manual dexterity, and somatosensory thresholds were assessed before and after 10-week training in 13 children with CP. Results: After 10-week training with the adapted serious game, children showed learning rates above 90% and improvement in motor learning parameters along the sessions. Manual dexterity and pronation-supination of the dominant hand improved after training. No significant effects were found on somatosensory thresholds. Conclusion: Serious games are useful as motor learning tools for improving motor function in children with PC. Cooperative work among professionals and users is advisable for designing efficient videogames according to rehabilitation best practices.

PMID: 37449840

8. Factor analysis of the Gait Outcomes Assessment List's goal questions: A new method to measure goal prioritization in ambulatory individuals with cerebral palsy

Meghan E Munger, Nathan D Shippee, Timothy J Beebe, Tom F Novacheck, Beth A Virnig

Dev Med Child Neurol. 2023 Jul 11. doi: 10.1111/dmcn.15704. Online ahead of print.

Aim: To evaluate the factor structure of the 49 goal prioritization questions of the Gait Outcome Assessment List (GOAL).

Method: This was a retrospective review of 622 consecutive individuals diagnosed with cerebral palsy (median = 11 years 2 months, SD = 6 years 0 months, 370 male), who underwent a routine clinical gait analysis at a specialty center and completed the validated GOAL. To assess dimensionality, we performed exploratory and confirmatory factor analyses on the goal ratings of its 49 gait-related items. For internal consistency, we calculated Cronbach's alpha. We created standardized goal scores for each factor and determined floor and ceiling effects according to the Gross Motor Function Classification System (GMFCS). Results: Factor analyses suggested that the GOAL's 49 goal prioritization items represented eight factors, one more than the original GOAL validation because pain and fatigue were separated into distinct factors. Cronbach alphas were acceptably high (\geq 0.80) across factors except for use of braces and mobility aids (α = 0.68). Goal importance varied across domains and GMFCS levels. Interpretation: The GOAL can be expanded as a tool to better understand goal priorities in ambulatory individuals with cerebral palsy. These scores can be used to guide clinical conversations and provide more focus than previously available when faced with 49 individual goals. Scores can also be aggregated across relevant populations for larger-scale studies.

PMID: 37431682

9. Design and Control of a Single-Leg Exoskeleton with Gravity Compensation for Children with Unilateral Cerebral Palsy

Mohammadhadi Sarajchi, Konstantinos Sirlantzis

Sensors (Basel). 2023 Jul 2;23(13):6103. doi: 10.3390/s23136103.

Children with cerebral palsy (CP) experience reduced quality of life due to limited mobility and independence. Recent studies have shown that lower-limb exoskeletons (LLEs) have significant potential to improve the walking ability of children with CP. However, the number of prototyped LLEs for children with CP is very limited, while no single-leg exoskeleton (SLE) has been developed specifically for children with CP. This study aims to fill this gap by designing the first size-adjustable SLE for children with CP aged 8 to 12, covering Gross Motor Function Classification System (GMFCS) levels I to IV. The exoskeleton incorporates three active joints at the hip, knee, and ankle, actuated by brushless DC motors and harmonic drive gears. Individuals with CP have higher metabolic consumption than their typically developed (TD) peers, with gravity being a significant contributing factor. To address this, the study designed a model-based gravity-compensator impedance controller for the SLE. A dynamic model of user and exoskeleton interaction based on the Euler-Lagrange formulation and following Denavit-Hartenberg rules was derived and validated in Simscape™ and Simulink® with remarkable precision. Additionally, a novel systematic simplification method was developed to facilitate dynamic modelling. The simulation results demonstrate that the controlled SLE can improve the walking functionality of children with CP, enabling them to follow predefined target trajectories with high accuracy.

PMID: 37447953

10. The temporal and bi-directional relationship between physical activity and sleep in ambulatory children with cerebral palsy

Anke Gerritsen, Raquel Y Hulst, Ilse M van Rijssen, Joyce Obeid, Sigrid Pillen, Jan Willem Gorter, Olaf Verschuren

Disabil Rehabil. 2023 Jul 9;1-7. doi: 10.1080/09638288.2023.2232720. Online ahead of print.

Purpose: Exploring the temporal and bi-directional relationship between device-based measures of physical activity and sleep in ambulatory children with cerebral palsy (CP). Materials and methods: 24-hour activity data were collected from children with CP (n = 51, 43% girls, mean age (range); 6.8 (3-12) years; Gross Motor Function Classification System levels I to III). Nocturnal sleep parameters and daily physical activity were measured for seven consecutive days and nights using ActiGraph GT3X accelerometers. Linear mixed models were constructed to explore the relationships between sleep and activity. Results: Light and moderate-to-vigorous activity were negatively associated with sleep efficiency (SE) (resp. p = 0.04, p = 0.010) and total sleep time (TST) (resp. p = 0.007, p = 0.016) the following night. Sedentary time was positively associated with SE and TST the following night (resp. p = 0.014, p = 0.004). SE and TST were positively associated with sedentary time (resp. p = 0.011, p = 0.001) and negatively with moderate-to-vigorous physical activity (resp. p = 0.004), the following day. Total bedtime and TST were negatively associated with light physical activity (resp. p = 0.046, p = 0.004) the following day. Conclusions: The findings from this study suggest that ambulatory children with CP may not sleep better after physical activity, and vice versa, indicating that the relationship is complex and needs further investigation.

PMID: 37424307

11. Response to: Zoledronate Increases Bone Mineral Density in Nonambulant Children With Cerebral Palsy: A Randomized, Controlled Trial

Anne Trinh, Frances Milat

Editorial J Clin Endocrinol Metab. 2023 Jul 12;dgad386. doi: 10.1210/clinem/dgad386. Online ahead of print.

No abstract available

PMID: <u>37437090</u>

12. Longitudinal Patterns of Postfracture Outpatient Physical Therapy and Occupational Therapy Use and Its Association With 3-Year Mortality Among Adults With Cerebral Palsy

Rachel E W Gottlieb, Kate V Panzer, Mia Wang, Aleda M Leis, Daniel G Whitney

Phys Ther. 2023 Jul 13;pzad090. doi: 10.1093/ptj/pzad090. Online ahead of print.

Objective: Fragility fractures are common among adults with cerebral palsy (CP), but clinical rehabilitation use after fracture and its effect on long-term health outcomes have not been sufficiently studied. The objectives of this study were to identify patterns of the use of physical therapy, occupational therapy, or both in the 6-month postfracture period and the association with 3-year mortality in adults with CP. Methods: This retrospective cohort study included adults who were ≥ 18 years old, had CP, and had sustained an incident fragility fracture between January 1, 2014, and December 31, 2016, as identified from a random 20% Medicare fee-for-service dataset. Six-month outpatient physical therapy or occupational therapy use patterns after fracture were identified using group-based trajectory modeling. Cox regression determined the association between physical therapy or occupational therapy use trajectory patterns and mortality from 6 months to 3 years after fracture, adjusting for confounders. Effect modification by key characteristics was tested, including age, sex, and the modified Whitney Comorbidity Index (mWCI), which is a CP-specific comorbidity index that better captures overall medical complexity. Results: Of the 2429 participants included, the majority (73.2%) were characterized as having little to no probability of physical therapy or occupational therapy use, while 16.0% and 10.7% were characterized as having early initiation and later initiation, respectively. Compared to the mortality rate for the little to no physical therapy or occupational therapy group, the mortality rates were 26% lower for the early physical therapy or occupational therapy initiation group (hazard ratio [HR] = 0.74; 95% CI = 0.55-1.00) and 20% lower for the later initiation group (HR = 0.80; 95% CI = 0.57-1.12). There was effect modification by the mWCI. The mortality rate was lower when the early initiation and later initiation groups were compared to the little to no initiation group across all mWCI values examined (median and interquartile range), but the effect was stronger (ie, lower mortality rate) for lower mWCI values for both early initiation and later initiation groups. Conclusions: Most adults with CP underutilize outpatient physical therapy or occupational therapy services within 6 months postfracture. Early or later initiation versus little to no physical therapy or occupational therapy use was associated with a lower HR of mortality, although the effect was stronger and statistically significant among those with less medical complexity.

PMID: 37440438

13. The Decline of Physical Activity with Age in School-Aged Children with Cerebral Palsy: A Single-Center Cross-Sectional Observational Study

Jinuk Lee, Min-Hwa Suk, Soojin Yoo, Jeong-Yi Kwon

J Clin Med. 2023 Jul 7;12(13):4548. doi: 10.3390/jcm12134548.

Maintaining physical activity is important for children with cerebral palsy (CP). This study examined whether age predicted habitual physical activity (HPA) or cardiorespiratory fitness (CRF) in school-aged children with CP and clarified the relationship between HPA and CRF. We utilized cross-sectional data from 39 children with CP (18 girls and 21 boys; mean age 7.44 years; mean body weight 24.76 kg; mean body mass index 15.97 kg/m2; hemiplegic or diplegic CP). The participants wore an accelerometer (ActiGraph) for five days to measure HPA, physical activity energy expenditure (kcal/kg/d), sedentary physical activity (%SPA), light physical activity, moderate-to-vigorous physical activity (%MVPA), and activity counts (counts/min). Participants underwent cardiopulmonary exercise tests on a treadmill using a modified Naughton protocol. Linear regression and correlation analyses were performed. p-value (two-tailed) < 0.05 was considered statistically significant. Age was positively associated with SPA. MVPA negatively correlated with resting heart rate (HR), and activity counts were negatively correlated with resting HR. In conclusion, our study found strong evidence of a negative association between HPA and age in school-aged children with CP. It highlights the importance of creating and improving recreational opportunities that promote physical activity in all children with CP, regardless of whether they are considered therapeutic.

PMID: <u>37445582</u>

14. Role of Vitalstim® In The Management Of Patients With Dysphagia: A MiniReview

Naima Farooq, Saleha Khatoon, Arshad Nawaz Malik, Farooq Azam Rathore

Review J Pak Med Assoc. 2023 Jun;73(6):1346-1348. doi: 10.47391/JPMA.23-46.

Dysphagia defined as difficulty in swallowing, can result from multiple causes including, Stroke, head injury, Alzheimer, Dementia, Muscular dystrophy, Cerebral Palsy etc. It is associated with neuro-muscular impairments in different age groups. VitalStim® therapy is a relatively new approach to treat dysphagia. It provides neuromuscular electrical stimulation (NMES) of the involved muscles to improve the function of swallowing. This review summarizes the usefulness of VitalStim® in dysphagia, and barriers in its use in Pakistan.

PMID: 37427651

15. [The content-analysis of normative legal regulation of medical social rehabilitation of children with infantile cerebral paralysis in the Russian Federation] [Article in Russian]

O N Golovina, I V Vinyarskaya

Probl Sotsialnoi Gig Zdravookhranenniiai Istor Med. 2023 May;31(3):360-367. doi: 10.32687/0869-866X-2023-31-3-360-367.

The infantile cerebral paralysis is a significant medical social problem and economic burden for family, health care system and state economy in general since such children require organization of accessible environment and life-long rehabilitation maintenance. The purpose of the study is content-analysis of normative legal regulation of medical social rehabilitation of children with infantile cerebral paralysis in the Russian Federation. The analysis of main normative legal documents established that medical social rehabilitation is implemented in concordance with norms of international legislation and is regulated by provisions of Federal laws and other normative legal acts of the Russian Federation and its subjects. It was established that despite noticeable progress the legislation in this area has a number of significant shortcomings that adversely affect accessibility for children with cerebral palsy of high-quality and effective services of comprehensive medical social rehabilitation and requires improvement.

PMID: 37427509

16. Comorbidities in children with cerebral palsy: a single-centre cross-sectional hospital-based study from India

Maya Viswanath, Ruchika Jha, Ankita Dilip Gambhirao, Arjun Kurup, Sachendra Badal, Sarvesh Kohli, Parvathi Parappil, Biju M John, Krishna Moorthi Adhikari, Uday Bhanu Kovilapu, Vishal Sondhi

BMJ Open. 2023 Jul 10;13(7):e072365. doi: 10.1136/bmjopen-2023-072365.

Objective: To describe the comorbidities in children with cerebral palsy (CP) and determine the characteristics associated with different impairments. Design: Cross-sectional study. Setting: Tertiary care referral centre in India. Patients: Between April 2018 and May 2022, all children aged 2-18 years with a confirmed diagnosis of CP were enrolled by systematic random sampling. Data on antenatal, birth and postnatal risk factors, clinical evaluation and investigations (neuroimaging and genetic/ metabolic workup) were recorded. Main outcome measures: Prevalence of the co-occurring impairments was determined using clinical evaluation or investigations as indicated. Results: Of the 436 children screened, 384 participated (spastic CP=214 (55.7%) (spastic hemiplegic=52 (13.5%); spastic diplegia=70 (18.2%); spastic quadriplegia=92 (24%)), dyskinetic CP=58 (15.1%) and mixed CP=110 (28.6%)). A primary antenatal/perinatal/neonatal and postneonatal risk factor was identified in 32 (8.3%), 320 (83.3%) and 26 (6.8%) patients, respectively. Prevalent comorbidities (the test used) included visual impairment (clinical assessment and visual evoked potential)=357/383(93.2%), hearing impairment (brainstem-evoked response audiometry)=113 (30%), no understanding of any communication (MacArthur Communicative Development Inventory)=137 (36%), cognitive impairment (Vineland scale of social maturity)=341 (88.8%), severe gastrointestinal dysfunction (clinical evaluation/interview)=90 (23%), significant pain (non-communicating children's pain checklist)=230 (60%), epilepsy=245 (64%), drug-resistant epilepsy=163 (42.4%), sleep impairment (Children's Sleep Habits Questionnaire)=176/290(60.7%) and behavioural abnormalities (Childhood behaviour checklist)=165 (43%). Overall, hemiparetic and diplegic CP and Gross Motor Function Classification System ≤3 were predictive of lesser co-occurring impairment. Conclusion: CP children have a high burden of comorbidities, which increase with increasing functional impairment. This calls for urgent actions to prioritise opportunities to prevent risk factors associated with CP and organise existing resources to identify and manage co-occurring impairments.

PMID: 37429681

17. Supportive mobility devices across the lifespan in Cerebral Palsy: a modified Delphi study to establish stakeholder research priorities

Heather A Feldner, Deborah Gaebler-Spira, Varun Awasthi, Kristie K Bjornson

Disabil Rehabil Assist Technol. 2023 Jul 15;1-9. doi: 10.1080/17483107.2023.2233564. Online ahead of print.

Purpose: The aim of this study was to co-develop research priorities and identify meaningful research questions with a diverse group of stakeholders representing the CP community for implementation in subsequent research activities. The overarching

aim of this research was to 1) Understand the mobility experiences, supported mobility device (SMD) use, and desired participation outcomes of people with cerebral palsy (CP) across the lifespan; and 2) Describe how perspectives of rehabilitation care and professional resources may influence mobility decision-making processes and outcomes. Materials and methods: A three-round modified Delphi consensus study was conducted with stakeholder advisory panel consisting of three adults with CP, two parents of children with CP, and four SMD providers. Results: The advisory panel identified 11 unique topical categories focused on SMD selection and use, stratified by age group and stakeholder role. Questions or statements within each category were ranked, and top consensus and concordance statements were retained, reviewed, and refined for use in a co-developed focus group guide. Priorities were identified in three main groupings: (1) Age/GMFCS level/Environment-related; (2) Individual with CP/Caregiver need-related; and (3) Clinician/provider partnership-related. Discussion: A modified Delphi process was a useful tool for stakeholders in co-developing research priorities related to SMD use across the lifespan. Drawing on the lived expertise of stakeholders is important in facilitating improved research translation in the CP community.

PMID: <u>3745257</u>5

18. Practice, play, repeat - individualized outcomes after the "intensity matters!"-program for children with disabilities - a descriptive multicase study

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Disabil Rehabil. 2023 Jul 14;1-6. doi: 10.1080/09638288.2023.2233905. Online ahead of print.

Purpose: To examine and categorize individual outcomes after the "Intensity matters!"-program, a new, cross-professional intensive intervention for children with disabilities across Norway. Materials and methods: 84 children and their parents/legal guardian were enrolled in this multicase study. Participants were active in defining goals, and hereby the content of the intervention. The pre-settled goals were grouped into the categories of body functions and structure, activities and participation inspired by the components of the International Classification of Functioning, Disability, and Health (ICF). The pre-settled goals were assessed pre- and post-intervention by using The Canadian Occupational Performance Measure (COPM). A clinically important change was predefined as a change ≥2 points. Results: 1004 pre-settled goals were categorized into focus areas, where 62.4% were categorized as activity; functional mobility (n = 626). Post-intervention assessment of the COPM ratings of child performance and satisfaction showed a mean change of 3.7 (range -0.25;8.5) and 3.8 (range 0.25;10), respectively. Conclusion: The majority of participants in the "Intensity Matters!"-program had a clinically important change in their individual goals after only three weeks of intervention. This study supports the use of client-centered measures in rehabilitation for children with disabilities, but a further examination of long-term outcome is warranted.

PMID: 37452469

19. Alterations in cortical morphometry of the contralesional hemisphere in children, adolescents, and young adults with perinatal stroke

Karan Shinde, Brandon T Craig, Jordan Hassett, Nomazulu Dlamini, Brian L Brooks, Adam Kirton, Helen L Carlson

Sci Rep. 2023 Jul 14;13(1):11391. doi: 10.1038/s41598-023-38185-8.

Perinatal stroke causes most hemiparetic cerebral palsy and cognitive dysfunction may co-occur. Compensatory developmental changes in the intact contralesional hemisphere may mediate residual function and represent targets for neuromodulation. We used morphometry to explore cortical thickness, grey matter volume, gyrification, and sulcal depth of the contralesional hemisphere in children, adolescents, and young adults after perinatal stroke and explored associations with motor, attention, and executive function. Participants aged 6-20 years (N = 109, 63% male) with unilateral perinatal stroke underwent T1-weighted imaging. Participants had arterial ischemic stroke (AIS; n = 36), periventricular venous infarction (PVI; n = 37) or were controls (n = 36). Morphometry was performed using the Computational Anatomy Toolbox (CAT12). Group differences and associations with motor and executive function (in a smaller subsample) were assessed. Group comparisons revealed areas of lower cortical thickness in contralesional hemispheres in both AIS and PVI and greater gyrification in AIS compared to controls. Areas of greater grey matter volume and sulcal depth were also seen for AIS. The PVI group showed lower grey matter volume in cingulate cortex and less volume in precuneus relative to controls. No associations were found between morphometry metrics, motor, attention, and executive function. Cortical structure of the intact contralesional hemisphere is altered after perinatal stroke. Alterations in contralesional cortical morphometry shown in perinatal stroke may be associated with different mechanisms of damage or timing of early injury. Further investigations with larger samples are required to more thoroughly explore associations with motor and cognitive function.

PMID: 37452141

20. Corticomuscular Coherence in Children with Unilateral Cerebral Palsy: A Feasibility and Preliminary Protocol Study

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Objective This study assessed the feasibility of corticomuscular coherence measurement during a goal-directed task in children with unilateral cerebral palsy while establishing optimal experimental parameters. Methods Participants (Manual Ability Classification System levels I-III) completed a submaximal isometric goal-directed grip task during simultaneous electroencephalography and electromyography (EMG) acquisition. Results All participants (n = 11, 6 females, mean age 11.3 ±2.4 years) completed corticomuscular coherence procedures. Of the 40 trials obtained per extremity, an average of 29 (n = 9) and 27 (n = 10) trials were retained from the more- and less-affected extremities, respectively. Obtaining measurement stability required an average of 28 trials per extremity. Conclusion Findings from this work support the feasibility of corticomuscular coherence measurement in children with unilateral cerebral palsy. Acquiring 28 to 40 corticomuscular coherence trials per extremity is ideal. The experimental parameters established in this work will inform future corticomuscular coherence application in pediatric unilateral cerebral palsy.

PMID: 37448333

21. Possibility for Children with Medical Complexities to Reach a 3000-m Peak: A Report of 2 Cases

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Case Reports Wilderness Environ Med. 2023 Jul 10;S1080-6032(23)00100-X. doi: 10.1016/j.wem.2023.05.008. Online ahead of print.

With the recent development of neonatal medicine, the number of children with medical complexities (CMCs) is increasing. Outdoor activities are important for their psychosocial development, and the principles of accessibility should be addressed. We report the experience of 2 CMCs' high-altitude mountaineering with the necessary support. The participants were a 3-y-old girl with cerebral palsy, symptomatic epilepsy, and a ventriculoperitoneal shunt (Child A) and a 6-y-old girl who underwent bilateral Glenn operations at 11 mo for hypoplastic left heart syndrome (Child B). The support staff consisted of 4 doctors, 1 nurse, 5 nonmedical staff, 3 members from a mountaineering association, and 2 people from an oxygen company. The climbing schedule was 2 days. On the first day, we took a bus to a hut at an altitude of 2450 m and stayed overnight to acclimatize to the altitude. On the second day, we took the beginner's route, which took 3 h to climb 500 m, and our team made an attempt on the summit. During the attempt, Child B panicked. Although her lung sounds did not raise suspicions of pulmonary edema, we decided to leave the mountain with her because her transcutaneous oxygen saturation decreased. Child A had no apparent health problems and made it to the summit. Although CMCs' alpine climbing requires careful planning and staffing considering the risk of high-altitude sickness, our case suggests the feasibility of such activities with CMCs as part of accessibility.

PMID: <u>37438154</u>

22. Nutritional interventions in children and adolescents with cerebral palsy: systematic review

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Objective: To systematically review the literature in search of the most suitable and effective nutritional interventions and indications for the nutritional treatment of children and adolescents with cerebral palsy (CP). Data source: This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The articles were selected from seven databases (Cochrane, Literatura Latino-Americana e do Caribe em Ciências da Saúde - Lilacs, Embase, United States National Library of Medicine - PubMed, Scientific Electronic Library Online - SciELO, Scopus, and Web of Science). Studies from a pediatric group (0 to 18 years old) diagnosed with CP were included and the search strategy included the descriptors: "children" OR "childhood" AND "nutritional therapy" OR "nutritional intervention" OR "nutrition" OR "nutritional support" OR "diet" AND "cerebral palsy" OR "cerebral injury". Methodological quality was assessed using the checklist for cross-sectional analytical studies, the Newcastle-Ottawa scale or the Cochrane Collaboration tool for clinical trials. Data synthesis: Fifteen studies (n=658) published from 1990 to 2020 met the inclusion criteria. All of them had a low risk of bias. The data showed that children and adolescents with CP have worse nutritional status than those normally developed. Those who received hypercaloric and hyperprotein nutritional supplementation benefited from its use. Studies indicate that enteral nutrition should be considered when nutritional needs are not met by the oral diet, especially in cases where oral motor functions are impaired. In addition, there was a direct relationship between the consistency of food, the

level of motor function and nutritional status. Conclusions: Children and adolescents with CP have a greater risk of malnutrition. The use of nutritional supplementation may help with weight gain. In addition, enteral nutrition and modification of food texture have been used to improve the nutritional status of this group.

PMID: 37436239

23. Circadian patterns of heart rate variability in fetal sheep after hypoxia-ischaemia: A biomarker of evolving brain injury

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Hypoxia-ischaemia (HI) before birth is a key risk factor for stillbirth and severe neurodevelopmental disability in survivors, including cerebral palsy, although there are no reliable biomarkers to detect at risk fetuses that may have suffered a transient period of severe HI. We investigated time and frequency domain measures of fetal heart rate variability (FHRV) for 3 weeks after HI in preterm fetal sheep at 0.7 gestation (equivalent to preterm humans) until 0.8 gestation (equivalent to term humans). We have previously shown that this is associated with delayed development of severe white and grey matter injury, including cystic white matter injury (WMI) resembling that observed in human preterm infants. HI was associated with suppression of time and frequency domain measures of FHRV and reduced their circadian rhythmicity during the first 3 days of recovery. By contrast, circadian rhythms of multiple measures of FHRV were exaggerated over the final 2 weeks of recovery, mediated by a greater reduction in FHRV during the morning nadir, but no change in the evening peak. These data suggest that the time of day at which FHRV measurements are taken affects their diagnostic utility. We further propose that circadian changes in FHRV may be a low-cost, easily applied biomarker of antenatal HI and evolving brain injury. KEY POINTS: Hypoxiaischaemia (HI) before birth is a key risk factor for stillbirth and probably for disability in survivors, although there are no reliable biomarkers for antenatal brain injury. In preterm fetal sheep, acute HI that is known to lead to delayed development of severe white and grey matter injury over 3 weeks, was associated with early suppression of multiple time and frequency domain measures of fetal heart rate variability (FHRV) and loss of their circadian rhythms during the first 3 days after HI. Over the final 2 weeks of recovery after HI, exaggerated circadian rhythms of frequency domain FHRV measures were observed. The morning nadirs were lower with no change in the evening peak of FHRV. Circadian changes in FHRV may be a low-cost, easily applied biomarker of antenatal HI and evolving brain injury.

PMID: 37432936

24. Impact of caregivers' psychological and caregiving status on recruitment, conversion, and retention in stem cell therapy trials for cerebral palsy: A prospective survey analysis

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Aim: To examine specific correlates that may affect retention outcomes of neural stem cell therapy trials in families screened for cerebral palsy. Design: A prospective correlational study. Methods: Primary caregivers completed surveys of psychological resilience, care burden and family caregiver tasks. The overall data and differences between groups were analysed and compared. Results: Resilience was negatively correlated with the care ability and closely related to the monthly household income and educational level of the caregivers. Factors affecting the final retention rate included the type of disease, number of combined disorders, monthly household income, primary caregivers' education level and resilience. Conclusion: Economic level, literacy and psychological status may affect trial retention. These findings can provide tips for preparing for subsequent screening, identification and intervention in stem cell clinical trials. Implication for the profession and/or patient care: The study results may provide nursing care tips to make recruitment more efficient, reduce trial costs, support patient-centredness and accelerate trial progress. No patient or public contribution: The target population involves the primary caregivers of children living with cerebral palsy. However, neither patients nor the public contributed to the design or conduct of the study, analysis, or interpretation of the data, or preparation of the manuscript.

PMID: 37431277

25. Youth engagement in research: exploring training needs of youth with neurodevelopmental disabilities

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Background: Authentic researcher-youth partnerships in patient-oriented research (POR) where the research responds to the needs expressed by youth themselves are essential to make research meaningful. While patient-oriented research (POR) is increasingly practiced, few training programs exist in Canada and none, to our knowledge, are tailored for youth with neurodevelopmental disabilities (NDD). Our primary objective was to explore the training needs of youth (ages 18-25) with NDD to enhance their knowledge, confidence, and skills as research partners. Our secondary objective was to identify the benefits and challenges of engaging youth with NDD in a POR approach. Methods: Our team of four youth and one parent with lived experience [Youth Engagement in Research (YER) partners] and six researchers engaged in POR to investigate the primary objective via two phases: (1) individual interviews with youth living with NDD and (2) a two-day virtual symposium with focus groups with youth and researchers. Collaborative qualitative content analysis was employed to synthesize the data. Our secondary objective was assessed by asking our YER partners to complete the Public and Patient Engagement Evaluation Tool (PPEET) survey and participate in reflective discussions. Results: Phase 1 participants (n = 7) identified various barriers and facilitators to their engagement in research and offered suggestions to meet their needs through minimizing barriers and integrating facilitators, which would subsequently enhance their knowledge, confidence, and skills as research partners. Informed by phase 1, phase 2 participants (n = 17) prioritized the following POR training needs: researcher-youth communication, research roles and responsibilities, and finding partnership opportunities. For delivery methods, participants stated the importance of youth representation, using Universal Design for Learning, and co-learning between youth and researchers. Based on the PPEET data and subsequent discussions, YER partners agreed that they were able to express views freely, feel that their views were heard, and that their participation made a meaningful difference. Challenges included scheduling difficulties, ensuring multiple methods for engagement, and working under short timelines. Conclusion: This study identified important training needs for youth with NDD and for researchers to engage in meaningful POR, which can subsequently inform the co-production of accessible training opportunities with and for youth.

PMID: 37430378

26. The potential of cell therapies for cerebral palsy: where are we today?

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No abstract available

PMID: 37428111

27. To guide future practice, perinatal trials should be much larger, simpler and less fragile with close to 100% ascertainment of mortality and other key outcomes

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The Australian Placental Transfusion Study (APTS) randomised 1,634 fetuses to delayed (\geq 60 s) versus immediate (\leq 10 s) clamping of the umbilical cord. Systematic reviews with meta-analyses, including this and similar trials, show that delaying clamping in preterm infants reduces mortality and need for blood transfusions. Amongst 1,531 infants in APTS followed up at two years, aiming to delay clamping for 60 s or more reduced the relative risk of the primary composite outcome of death or disability by 17% (p = 0.01). However, this result is fragile because nominal statistical significance (p < 0.05) would be abolished by only 2 patients switching from a non-event to an event, and the primary composite outcome was missing in 112 patients (7%). To achieve more robust evidence, any future trials should emulate the large, simple trials co-ordinated from Oxford which reliably identified moderate, incremental improvements in mortality in tens of thousands of participants, with <1% missing data. Those who fund, regulate, and conduct trials that aim to change practice should repay the trust of those who consent to participate by doing everything possible to minimise missing data for key outcomes.

PMID: 37422415

28. Influence of the percutaneous myofasciotomy on gait of children with spastic cerebral palsy - A short term, retrospective controlled analysis

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Gait Posture. 2023 Jun 30;104:159-164. doi: 10.1016/j.gaitpost.2023.06.023. Online ahead of print.

Background: One of the primary causes in children with cerebral palsy (CP) leading to gait disorders is an increased muscle tone which may secondary result in a shortening of the muscle fascia. Percutaneous myofasciotomy (pMF) is a minimal-

invasive surgical intervention correcting the shortened muscle fascia and aims to extend the range of motion. Research question: What is the effect of pMF on gait in children with CP three months and one year post-OP? Methods: Thirty-seven children (f: n=17, m: n=20; age: 9.1 ± 3.9 years) with spastic CP (GMFCS: I-III, bilateral (BSCP): n=24, unilateral (USCP): n=13) were retrospectively included. All children underwent a three dimensional gait analysis with the Plug-in-Gait-Model before (T0) and three months after pMF (T1). Twenty-eight children (bilateral: n=19, unilateral: n=9) underwent a one-year follow-up-measurement (T2). Differences in the Gait Profile Score (GPS), kinematic gait data, gait-related functions and mobility in daily living were statistically analyzed. Results were compared to a control group (CG) matched in age (9.5 ± 3.5 years), diagnosis (BSCP: n=17; USCP: n=8) and GMFCS-level (GMFCS I-III). This group was not treated with pMF but underwent two gait analyses in twelve months. Results: The GPS improved significantly in BSCP-pMF ($16.46\pm3.71^{\circ}$ to $13.37\pm3.19^{\circ}$; p<0.001) and USCP-pMF ($13.24\pm3.27^{\circ}$ to $10.16\pm2.06^{\circ}$; p=0.003) from T0 to T1 with no significant difference between T1 and T2 in both groups. In CG there was no difference in the GPS between the two analyses. Significance: PMF may in some children with spastic CP improve gait function three months as well as for one-year post-OP. Medium and long-term effects, however, remain unknown and further studies are needed.

PMID: 37421812

Prevention and Cure

29. SuPreme Study: a protocol to study the neuroprotective potential of sulfate among very/extremely preterm infants

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Introduction: Antenatal maternal magnesium sulfate (MgSO4) administration is a proven efficacious neuroprotective treatment reducing the risk of cerebral palsy (CP) among infants born preterm. Identification of the neuroprotective component with target plasma concentrations could lead to neonatal treatment with greater efficacy and accessibility. Methods and analysis: This is a prospective observational cohort study, in three tertiary Australian centres. Participants are preterm infants, irrespective of antenatal MgSO4 exposure, born in 2013-2020 at 24+0 to 31+6 weeks gestation, and followed up to 2 years corrected age (CA) (to September 2023). 1595 participants are required (allowing for 17% deaths/loss to follow-up) to detect a clinically significant reduction (30% relative risk reduction) in CP when sulfate concentration at 7 days of age is 1 SD above the mean. A blood sample is collected on day 7 of age for plasma sulfate and magnesium measurement. In a subset of participants multiple blood and urine samples are collected for pharmacokinetic studies, between days 1-28, and in a further subset mother/infant blood is screened for genetic variants of sulfate transporter genes. The primary outcome is CP. Surviving infants are assessed for high risk of CP at 12-14 weeks CA according to Prechtl's Method to assess General Movements. Follow-up at 2 years CA includes assessments for CP, cognitive, language and motor development, and social/behavioural difficulties.Multivariate analyses will examine the association between day 7 plasma sulfate/magnesium concentrations with adverse neurodevelopmental outcomes. A population pharmacokinetic model for sulfate in the preterm infant will be created using non-linear mixed-effects modelling. Ethics and dissemination: The study has been approved by Mater Misericordiae Ltd Human Research Ethics Committee (HREC/14/MHS/188). Results will be disseminated in peer-reviewed journal publications, and provided to the funding bodies. Using consumer input, a summary will be prepared for participants and consumer groups.

PMID: 37451710